

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

Claim 1 (previously canceled)

Claim 2 (previously canceled)

Claim 3 (previously canceled)

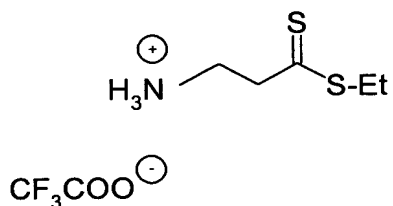
Claim 4 (previously canceled)

Claim 5 (previously canceled)

Claim 6 (previously amended) A method according to claim 35, wherein said coupling is a classical peptide coupling using a derivative of 2-(2-nitro-imidazol-1-yl) acetic acid in which the OH group of the carboxyl function has been replaced by a good leaving group.

Claim 7 (currently amended) A method for the synthesis of a compound according to claim 31 ~~or the corresponding non-labeled form thereof~~, comprising the steps of:

- adding a THF solution of 2 of Figure 7 to a suspension of PYBOP in THF followed by Et₃N,
- adding an amine 4 of Figure 7 formula 1



and Et₃N to the solution obtained in step (a),

- c) adding a catalytic amount to the solution obtained in step (b) of pTsOH and refluxing the solution,
- d) cooling the solution obtained after step (c) at ambient temperature and adding a sodium bicarbonate solution,
- e) extracting the product obtained after step (d) with ethyl acetate and drying and concentrating the product with ethyl acetate,
- f) purifying the residue obtained after step (e) by column chromatography on silica gel,
- g) removing traces of water by washing the product of step (f) with trifluoroacetic anhydride,
- h) reacting ~~said~~ a persulphurated derivative obtained from step (g) with a suitable labeled ~~or non~~ ~~labeled~~ perfluorinating agent and a suitable oxidant resulting in a compound having a high yield of fluor atom incorporation,
- i) deprotecting the nitrogen function, resulting in a perfluoroalkyl amine derivative, and
- j) coupling the perfluoroalkyl amine derivative obtained in step (i) with an activated form of 2-(2-nitro-imidazol-1-yl) acetic acid, resulting in the [18F]-labeled or ~~non-labelled~~ perfluorinated-nitroaromatic compound.

Claim 8 (original) A method according to claim 7 wherein hydrogen fluoride/pyridine complex (HF-Pyridine) is used as a perfluorinating agent and 1,3-dibromo-5,5-dimethylhydantoin (DBH) is used as an oxidant resulting in a compound having a high yield of fluor atom incorporation.

Claim 9 (cancel)

Claim 10 (original) A first intermediate compound having the general formula of an amino acid derivative which is N-protected by an imido group or a synthetically equivalent group and wherein the carboxyl function has been transformed into a dithioester function or a synthetically equivalent persulphurated moietyl.

Claim 11 (original) A first intermediate compound according to claim 10, wherein the imido group is a phthalimido group.

Claim 12 (previously amended) A first intermediate compound according to claim 10, obtainable via steps a to g of the method of the invention.

Claim 13 (previously amended) A first intermediate compound according to claim 10, being ethyl 3-(N-phthalimido)-aminopropanedithioate, N-3,3,3-trifluoro-2-thioxopropyl) phthalimide, N-{[2-(trifluoromethyl)-1, 3-dithiolan-2-yl] methyl} phthalimide, methyl(or ethyl) 3-phthalimide-2,2-difluoropropanedithioate, N-[2,2-difluoro-3,3,3-tris(methylthio) propyl] phthalimide or N-[2,2-difluoro-3,3,3-tris(ethylthio)propyl] phthalimide.

Claim 14 (original) A second intermediate compound having the general formula of a [^{18}F]-labelled perfluorinated amino acid derivative which is N-protected by an imido group or a synthetically equivalent group.

Claim 15 (original) A second intermediate compound according to claim 14, wherein the imido group is a phthalimido group.

Claim 16 (previously amended) A second intermediate compound according to claim 14, obtainable via steps a to h of the method of the invention.

Claim 17 (previously amended) A second intermediate compound according to claim 14, being N-(3,3,3-trifluoropropyl)phthalimide.

Claim 18 (original) A third intermediate compound having the general formula of a [^{18}F]-labelled perfluoroalkyl amine.

Claim 19 (original) A third intermediate compound according to claim 18, being [^{18}F]-labelled 3,3,3-trifluoropropyl amime.

Claim 20 (previously amended) A third intermediate [^{18}F]-labeled compound obtainable via steps a to i of the method of the invention.

Claim 21 (cancel)

Claim 22 (previously amended) A [^{18}F] labeled bioactive compound synthesized using as intermediates a first and third intermediate as claimed in claim 10, a second intermediate having the general formula of a [^{18}F]-labeled perfluorinated amino acid derivative which is N-protected by an imido group or a synthetically equivalent group.

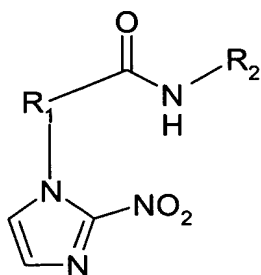
Claim 23 (previously amended) A [^{18}F] labeled bioactive compound synthesized using as intermediates a first intermediate as claimed in claim 10.

Claim 24 (previously amended) Method of perfluorination using as an intermediate a compound as claimed in claim 10.

Claim 25 (original) The compound of claim 22 which is an [^{18}F]-labeled perfluorinated nitroimidazole compound having an incorporation of [^{18}F] atoms characterized by a specific radioactivity of the compound comprised between 1 and 30 Ci/mmol, preferably between 1 and 20 Ci/mmol, preferably 1 and 10 Ci/mmol.

Claim 26 (currently amended) A method for the detection of tissue hypoxia in a patient comprising:

- producing a [^{18}F]-labeled perfluorinated-nitroaromatic compound having the formula:



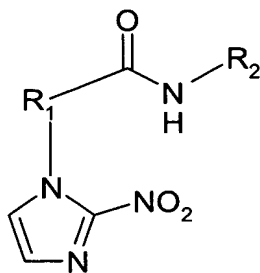
wherein R_1 is CH_2 and R_2 is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula $CHXCX_2CY_3$ where X is halogen or hydrogen and Y is fluorine by coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [^{18}F]-labeled perfluoroalkyl amine derivative;

- introducing an [^{18}F] labeled nitroimidazole compound of claim 31 into said patient,
- imaging tissue hypoxia in said patient, and
- quantifying tissue hypoxia in said patient.

Claim 27 (original) A method according to claim 26 wherein the detection technique used in said method is positron emission tomography.

Claim 28 (currently amended) A method for the detection of tissue hypoxia in a tissue comprising:

- producing a [^{18}F]-labeled perfluorinated-nitroaromatic compound having the formula:



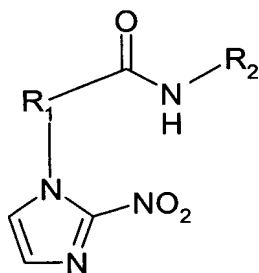
wherein R_1 is CH_2 and R_2 is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula $CHXCX_2CY_3$ where X is halogen or hydrogen and Y is

fluorine by coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [^{18}F]-labeled perfluoroalkyl amine derivative;

- introducing ~~an~~ said [^{18}F] labeled nitroimidazole compound of claim 31 into a patient,
- removing a tissue sample from said patient, and
- analysing the emission in said tissue sample by autoradiography.

Claim 29 (currently amended) A method for the detection of an [^{18}F] labeled bioactive compound in a patient comprising:

- producing a [^{18}F]-labeled perfluorinated-nitroaromatic compound having the formula:

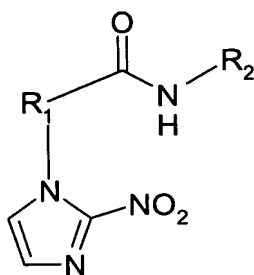


wherein R_1 is CH_2 and R_2 is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula $\text{CHXCX}_2\text{CY}_3$ where X is halogen or hydrogen and Y is fluorine by coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [^{18}F]-labeled perfluoroalkyl amine derivative;

- introducing ~~an~~ said [^{18}F] labeled bioactive compound according to claim 31 into said patient,
- imaging the presence of said [^{18}F] labeled bioactive compound in said patient, and
- optionally, quantifying the presence of said [^{18}F] labeled bioactive compound in said patient.

Claim 30 (currently amended) A method for the detection of [^{18}F] labeled bioactive compound in a tissue comprising:

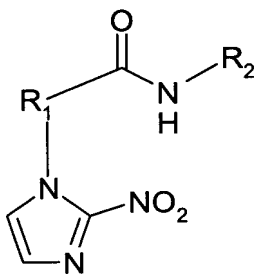
- producing a [^{18}F]-labeled perfluorinated-nitroaromatic compound having the formula:



wherein R_1 is CH_2 and R_2 is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula $CHXCX_2CY_3$ where X is halogen or hydrogen and Y is fluorine by coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [^{18}F]-labeled perfluoroalkyl amine derivative;

- introducing an [^{18}F] labeled bioactive compound of claim 31 into a patient,
- taking a tissue sample from said patient, and
- analysing the emission in said tissue sample by autoradiography.

Claim 31 (currently amended) A method for the synthesis of a [^{18}F]-labelled perfluorinated-nitroaromatic compound having the formula:



wherein R_1 is CH_2 and R_2 is an alkyl group having up to about 6 halogen atoms, wherein said alkyl group has the formula $CHXCX_2CY_3$ where X is halogen or hydrogen and Y is fluorine, comprising coupling 2-(2-nitro-imidazol-1-yl) acetic acid with a [^{18}F]-labeled perfluoroalkyl amine derivative.

Claim 32 (**currently amended**) A ~~compound~~ method according to claim 31, ~~having~~
wherein the compound has a specific radioactivity of the compound comprised between of 1 and to
30 Ci/mmol, ~~preferably between 1 and 20 Ci/mmol, preferably between 1 and 10 Ci/mmol.~~

Claim 33 (**currently amended**) A ~~compound~~ method according to claim 31, ~~having~~
wherein the compound has the formula 2-(2-nitro-1H-imidazol-1-yl)-N-(3,3,3-trifluoropropyl)
acetamide ([¹⁸F]-EF3).

Claim 34 (**currently amended**) A ~~compound~~ method according to claim 32, ~~having~~
wherein the compound has the formula 2-(2-nitro-1H-imidazol-1-yl)-N-2,2,3,3,3-pentafluoropropyl)
acetamide ([¹⁸F]-EF5).

Claim 35 (**cancel**)